

Attorney Docket No.: **FBR0002US.NP**
Inventors: **Dalby-Payne et al.**
Serial No.: **Not yet assigned**
Filing Date: **Herewith**
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This listing of the claims will replace all prior versions and listings of claims in the application:

Listing of the claims:

Claims 1-43: (cancelled)

Claim 44: (new) A method of screening for a compound that regulates an activity of a cell surface protein, the method comprising analysing an activity or cellular location of tropomyosin, expression levels of tropomyosin, or binding of tropomyosin to one of its binding partners in the presence of a candidate compound, wherein altered tropomyosin activity or cellular location, altered expression levels of tropomyosin or an altered level of binding of tropomyosin to its binding partner in the presence of the compound indicates that the compound regulates the activity of a cell surface protein.

Claim 45: (new) The method of claim 44 wherein altered cellular location of tropomyosin in the presence of the compound indicates that the compound increases the activity of a cell surface protein.

Claim 46: (new) The method of claim 44 wherein reduced tropomyosin expression in the presence of the compound indicates that the compound increases the activity of a cell surface protein.

Claim 47: (new) The method of claim 44 wherein a reduced level of binding of tropomyosin to its binding partner in the presence of

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the compound indicates that the compound increases the activity of a cell surface protein.

Claim 48: (new) The method of claim 44 wherein the tropomyosin binding partner is selected from the group consisting of calponin, CEACAM1, endostatin, Enigma, Gelsolin, S100A2 and actin.

Claim 49: (new) The method of claim 48 wherein the tropomyosin binding partner comprises sub-domain 2 of Gelsolin.

Claim 50: (new) The method of claim 44 wherein the cell surface protein is selected from the group consisting of a transport protein, a channel, a receptor, a growth factor, an antigen, a signalling protein and a cell adhesion protein.

Claim 51: (new) The method of claim 44 wherein the protein is a transport protein or a channel.

Claim 52: (new) The method of claim 44 wherein the tropomyosin is a tropomyosin isoform comprising an amino acid sequence encoded by exon 1b of a TPM 1 gene (SEQ ID NO:11) or an amino acid sequence encoded by exon 1b of a TPM 3 gene (SEQ ID NO:12).

Claim 53: (new) The method of claim 44 wherein the tropomyosin is a tropomyosin isoform TM5a or TM5b.

Claim 54: (new) A method of screening for a therapeutic compound for treatment of cystic fibrosis, the method comprising

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analysing an activity or cellular location of tropomyosin, expression levels of tropomyosin or binding of tropomyosin to one of its binding partners in the presence of a candidate compound, wherein altered tropomyosin activity or cellular location, altered expression levels of tropomyosin or an altered level of binding of tropomyosin to its binding partner in the presence of the compound indicates that the compound is useful for treatment of cystic fibrosis.

Claim 55: (new) The method of claim 54 wherein altered cellular location of tropomyosin in the presence of the compound indicates that the compound is useful for treatment of cystic fibrosis.

Claim 56: (new) The method of claim 54 wherein reduced tropomyosin expression in the presence of the compound indicates that the compound is useful for treatment of cystic fibrosis.

Claim 57: (new) The method of claim 54 wherein a reduced level of binding of tropomyosin to its binding partner in the presence of the compound indicates that the compound is useful for treatment of cystic fibrosis.

Claim 58: (new) The method of claim 54 wherein the tropomyosin binding partner is selected from the group consisting of calponin, CEACAM1, endostatin, Enigma, Gelsolin, S100A2 and actin.

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Claim 59: (new) The method of claim 58 wherein the tropomyosin binding partner comprises sub-domain 2 of Gelsolin.

Claim 60: (new) The method of claim 54 wherein the tropomyosin is a tropomyosin isoform comprising an amino acid sequence encoded by exon 1b of the TPM 1 gene (SEQ ID NO:11) or an amino acid sequence encoded by exon 1b of the TPM 3 gene (SEQ ID NO:12).

Claim 61: (new) The method of claim 54 wherein the tropomyosin is a tropomyosin isoform TM5a or TM5b.

Claim 62: (new) The method of claim 54 further comprising formulating the compound for administration to a human or a non-human animal.

Claim 63: (new) A method for regulating insertion or retention of a protein in a cell surface membrane, the method comprising administering to a cell an agent that modulates tropomyosin expression, location or activity.

Claim 64: (new) The method of claim 63 wherein the insertion or retention of the protein in the cell surface membrane is increased by administering a tropomyosin antagonist to the cell.

Claim 65: (new) The method of claim 63 wherein the protein is selected from the group consisting of a transport protein, a channel, a receptor, a growth factor, an antigen, a signalling protein and a cell adhesion protein.

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Claim 66: (new) The method of claim 65 wherein the transport protein is cystic fibrosis transmembrane conductance regulator (CFTR).

Claim 67: (new) The method of claim 63 wherein the tropomyosin is a tropomyosin isoform comprising an amino acid sequence encoded by exon 1b of the TPM 1 gene (SEQ ID NO:11) or an amino acid sequence encoded by exon 1b of the TPM 3 gene (SEQ ID NO:12).

Claim 68: (new) The method of claim 63 wherein the tropomyosin is a tropomyosin isoform TM5a or TM5b.

Claim 69: (new) The method of claim 64 wherein the tropomyosin antagonist is an antisense compound, a catalytic molecule or an RNAi molecule directed against tropomyosin-encoding mRNA.

Claim 70: (new) The method of claim 64 wherein the tropomyosin antagonist is an antisense compound, a catalytic molecule or an RNAi molecule targeted specifically against exon 1b of a TPM 1 gene (SEQ ID NO:7) or exon 1b of a TPM 3 gene (SEQ ID NO:8).

Claim 71: (new) The method of claim 64 wherein the tropomyosin antagonist is an antisense compound, a catalytic molecule or an RNAi molecule targeted to a sequence AGCTCGCTGGAGGCGGTG (SEQ ID NO:13).

Claim 72: (new) A method for the treatment or prevention of cystic fibrosis in a subject, the method comprising administering

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to a subject an agent that modulates tropomyosin expression, location or activity.

Claim 73: (new) The method of claim 72 wherein the tropomyosin is a tropomyosin isoform comprising an amino acid sequence encoded by exon 1b of the TPM 1 gene (SEQ ID NO:11) or an amino acid sequence encoded by exon 1b of the TPM 3 gene (SEQ ID NO:12).

Claim 74: (new) The method of claim 72 wherein the tropomyosin is a tropomyosin isoform TM5a or TM5b.

Claim 75: (new) The method of claim 72 wherein the agent that modulates tropomyosin expression, location or activity is an antisense compound, a catalytic molecule or an RNAi molecule directed against tropomyosin-encoding mRNA.

Claim 76: (new) The method of claim 72 wherein the agent that modulates tropomyosin expression, location or activity is an antisense compound, a catalytic molecule or an RNAi molecule targeted specifically against exon 1b of s TPM 1 gene (SEQ ID NO:7) or exon 1b of a TPM 3 gene (SEQ ID NO:8) .

Claim 77: (new) The method of claim 72 wherein the agent that modulates tropomyosin expression, location or activity is an antisense compound comprising a sequence CACCGCCUCCAGCGAGCT (SEQ ID NO:14) .